ELSEVIER

Journal of Fluorine Chemistry 107 (2001) 315–319

JOURNAL OF FLUORINE CHEMISTRY

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Synthesis of 2-trifluoromethylthioacrylate and its derivatives via the Knoevenagel condensation

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Received 3 April 2000; accepted 6 April 2000

Abstract

Ethyl 3-aryl and 3-alkyl-2-(trifluoromethylthio)acrylates as well as 2-(trifluoromethylthio)acrylate (**3**) are readily prepared by the Knoevenagel condensation of ethyl (trifluoromethylthio)acetate (**2**) with aldehydes under mild conditions.

Keywords: Trifluoromethylthio; Acrylates; Knoevenagel condensation; Aldehydes

1. Introduction

Despite the interesting and particular properties of the trifluoromethylthio moiety [1], only a modest number of CF_3S-substituted compounds have been synthesized. Vinyl SCF_3 systems, although structurally simple, are even less well known. They may, however, find potential use in the preparation of polymers for example as core materials for optical waveguides [2].

Free-radical addition of trifluoromethanesulfenyl chloride (CF_3SCl) to methyl acrylate with subsequent elimination of hydrogen chloride was shown to afford a mixture of 2- and 3-trifluoromethylthioacrylate regioisomers and a bis adduct [3]. In the presence of excess CF_3SCl, disubstitution of triethyl orthoacetate was observed, giving 1,1,1-triethoxy-2,2-bis(trifluoromethylthio)ethane which underwent thermal elimination to yield 1,1-diethoxy-2,2-bis(trifluoromethylthio)ethene [4]. Trifluoromethanesulfenyl chloride, however, is both highly toxic and expensive. Finally, condensation of 2-(trifluoromethylthio)acetonitrile with 1,1,3,3-tetramethoxypropane was found to give a mixture of 3-(2,2-dimethoxyethyl)-α-trifluoromethylthiocyanoacrylate and the corresponding methanol elimination product [5].

In an effort to develop a new synthesis of α-(trifluoromethylthio)acrylates, we studied the Knoevenagel reaction with ethyl (trifluoromethylthio)acetate.

The Knoevenagel condensation of sulfur substituted nucleophiles to afford thioacrylates remains relatively unexplored [6]. For example, β-cyanoarylsulfides and α-(arylthio)carboxylate esters undergo condensation with a number of aromatic aldehydes and ketones in modest yield in the presence of potassium *tert*-butoxide or lithium amides [7–10]. Likewise, α-(*o*-nitrophenylthio)cinnamate was obtained by reacting methyl (*o*-nitrophenylthio)acetate and a variety of aryl aldehydes, in the presence of piperidine [11].

On the other hand, 3-aryl-2-(perfluoroalkanesulfonyl)-acrylates have been recently prepared in our laboratory by the Knoevenagel reaction of ethyl (trifluoromethanesulfonyl)acetate [12].

In this paper, we now report the direct and efficient preparation of ethyl 3-aryl and 3-alkyl-2-(trifluoromethylthio)acrylates (**3**) by the Knoevenagel condensation of ethyl (trifluoromethylthio)acetate (**2**) with various aromatic and aliphatic aldehydes **1**.

2. Results and discussion

2.1. Preparation of ethyl β-aryl or alkyl α-(trifluoromethylthio)acrylate

We initially supposed that condensation between an aldehyde and **2** could be performed through generation of the anion of **2** with a strong base (LDA, −78°C). This procedure has already been used for example in the condensation of fluorosulfides with carbonyl electrophiles [13].

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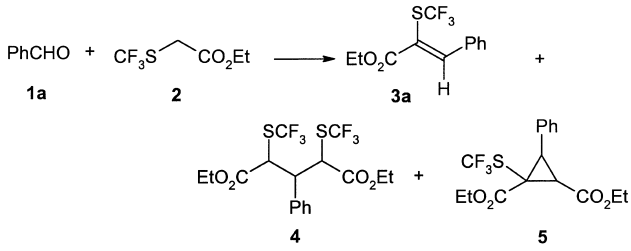
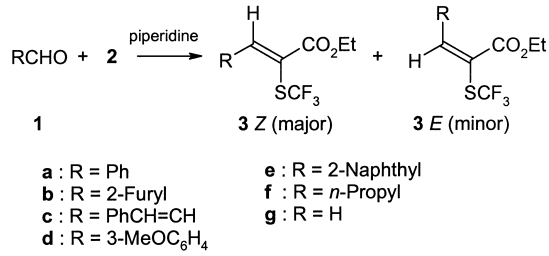
0022-1139/01/$ – see front matter
PII: S0022-1139(00)00375-4



Scheme 1.



Scheme 2.

In our preliminary trials, benzaldehyde was employed as the electrophile (Scheme 1). Although under these conditions the expected product **3a** was produced in 29% yield, the purification was complicated by the formation of the Michael addition and cyclopropanation adducts **4** and **5** (Table 1) (entry 1). Compound **5** is probably formed by deprotonation of **4α** to an ester group followed by cyclisation with departure of a trifluoromethanethiolate anion.

The condensation was subsequently attempted, under Knoevenagel conditions, in the presence of a catalytic quantity of piperidinium acetate in toluene, but without a greater level of success (entry 2).

Knoevenagel condensation was eventually achieved in moderate to good yields and in the absence of side products, in the presence of sub-stoichiometric quantities of piperidine (entry 3) [14].

In a typical procedure, treatment of one equivalent of ethyl (trifluoromethylthio)acetate and one equivalent of an aldehyde with 0.5 equivalents of piperidine as catalyst, in acetonitrile at reflux, gave the product **3**. Having optimised the conditions, the condensation was repeated for a series of aldehydes (Scheme 2 and Table 2).

The mechanism belongs to the class of base-catalysed aldol-type condensations. Employing piperidine as catalyst, the condensation of the aldehyde and the amine is considered to occur via the iminium salt of the carbonyl component, subsequent to which further dehydration of the adduct then forms the final olefin [6].

Aliphatic aldehydes like butyraldehyde led to the desired product but in only a modest yield (entry 6). On the other hand, condensation of ketones such as acetophenone did not proceed. The condensation products **3a–f** were characterized by their spectral data. In particular the $^{3}J_{(C=O,H)}$ coupling constant of 6 Hz measured in the proton-coupled ^{13}C NMR spectra of the major isomer of **3a** was in agreement with the predicted value for a double bond with a *Z*-configuration, that is with the aryl group *cis* to the trifluoromethylthio moiety. Equally, a coupling of 12 Hz for the minor isomer of **3a** (see Section 3) is characteristic of the opposite *E*-configuration [15]. In general, the NMR data for each of the major isomers of the compounds **3a–f** are consistent with the formation of the *Z*-alkene (Table 2). This is in contrast with the analogous alkenes obtained via the Knoevenagel condensation of sulfonyl [12] and sulfinyl [14] nucleophiles. Under the conditions employed, the stereoselectivity of the condensation is presumed to be governed by steric effects [14]. Hence, the results described above suggest that whilst both trifluoromethylsulfone and sulfoxide moieties are more bulky than the ester, the trifluoromethylthio is less sterically demanding.

2.2. Preparation of ethyl α-(trifluoromethylthio)acrylate

The Knoevenagel condensation of ethyl (trifluoromethylthio)acetate with paraformaldehyde was also successful, but under slightly modified conditions. Under reflux in acetonitrile, the end product **3g** appears to undergo a decomposition and/or a polymerisation. At room temperature, and with an excess of piperidine and paraformaldehyde, we obtained the intermediary amino-compound **6**. In this particular case, the conversion of the amine addition compound to the Knoevenagel adduct took place during the column chromatography. It involved the use of more than a catalytic amount of piperidine (Scheme 3).

3. Experimental

NMR spectra were recorded unless otherwise stated as $CDCl_3$ solutions, on a Bruker AC-300 spectrometer.

Table 1
Condensation of **1a** with **2**[a]

Entry	Conditions	**2** (%)	**3a** (%)[b]	**4** (%)[c]	**5** (%)	Unidentified (%)
1	LDA, THF, −78°C to room temperature, then benzene reflux	5	26	53	15	1
2	Piperidine, acetic acid room temperature, then toluene, reflux	41	20	0	0	39
3	Piperidine, MeCN, reflux	31	69	0	0	0

[a] Variation of reaction conditions. Composition determined by ^{19}F NMR spectroscopy.
[b] Mixture of *Z*- and *E*-isomers.
[c] Mixture of diastereoisomers.

Table 2
Knoevenagel adducts of **2**

Entry	Product	*Z*/*E*[a]	Yield (%)[b]	$^3J_{C=O,H}$[c] (Hz)	$\delta_{H,Acrylic}$ (ppm)
1	**3a**	90/10	54	6	7.85
2	**3b**	98/2	56	6	8.20
3	**3c**	97/3	53	5	8.15
4	**3d**	95/5	38	6	8.40
5	**3e**	99/1	34	6	8.60
6	**3f**	96/4	19	5	7.70
7	**3g**	–	36	6[d]	6.36 and 6.88

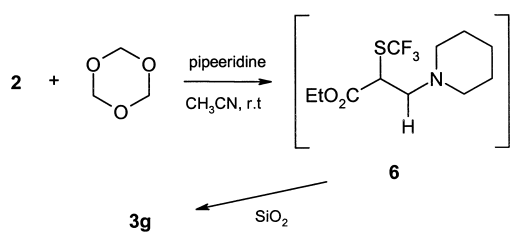
[a] Ratio determined by ^{19}F NMR analysis of the crude mixture.
[b] Isolated yields of *Z*-isomer.
[c] For the *Z*-isomer.
[d] $^3J_{C=O,H\,cis} \cdot {}^3J_{C=O,H\,trans} = 12$ Hz. Coupling constants were determined with simultaneous selective decoupling of the CH_2CH_3 protons.

Reported coupling constants and chemicals shifts were based on a first order analysis. Internal reference was the residual peak of $CHCl_3$ (7.27 ppm) for ^{1}H (300 MHz), central peak of $CDCl_3$ (77 ppm) for ^{13}C (75 MHz) spectra and internal $CFCl_3$ (0 ppm) for ^{19}F (282 MHz) NMR spectra. IR spectra were recorded as CCl_4 solutions on an Impact 400D Nicolet spectrophotometer. High resolution mass spectra were performed with a Finnigan MAT 95S spectrometer. Boiling points were determined by the Siwoloboff method on a Buchï melting point apparatus.

Ethyl (trifluoromethylthio)acetate (**2**) was prepared from ethyl mercaptoacetate and CF_3Br [16].

*3.1. Reaction of ethyl (trifluoromethylthio)acetate (**2**) with benzaldehyde induced by LDA*

A solution of ethyl (trifluoromethylthio)acetate (**2**) (400 mg, 2.1 mmol) in THF (5 ml) was added to a solution of lithium diisopropylamide (prepared from a solution of 2.3 mmol of diisopropylamine in 30 ml THF and 2.4 mmol of lithium *n*-butyl in hexanes under nitrogen) cooled to −23°C. After 30 min of stirring at −23°C, the solution was further cooled to −78°C and benzaldehyde (0.22 ml, 2.2 mmol) was added. The reaction mixture was stirred for 3 h and the temperature was slowly raised to 20°C. The mixture was hydrolyzed by addition of an aqueous solution of ammonium chloride and extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), and concentrated. The residue dissolved in benzene, was refluxed for 4 h with a water trap (Dean-Stark), until no further water separated. The solvent was removed under pressure. The oily residue (600 mg) was shown by ^{19}F NMR to contain: **3a** (*Z*) (−41.3 ppm, 24%), **3a** (*E*) (−42.7 ppm, 2%), **5** (−40.3 ppm, 15%), **4a** (−40.4 and −41.0 ppm, 29%), **4b** (−40.42 ppm, 15%), **4c** (−41.0 ppm, 9%), **2** (−42.8 ppm, 5%). Samples of each compound were obtained by flash chromatography (silica-gel; pentane/dichloromethane solvent gradient).



Scheme 3.

Diethyl 1-trifluoromethylthio-3-phenyl-cyclopropane-1,2-dicarboxylate (**5**). Oil, bp 250°C (Siwoloboff, dec.). HRMS 362.0792, $C_{16}H_{17}F_3O_4S$ requires 362.0799. ^{1}H NMR δ: 1.32 (3H, t, $J = 7.2$ Hz, CH_3); 1.33 (3H, t, $J = 7.2$ Hz, CH_3); 2.98 (1H, d, $J = 7.9$ Hz, C*H*Ph); 3.72 (1H, d, $J = 7.9$ Hz, C*H*CO_2Et); 4.26 (4H, m, OCH_2); 7.27 (2H, m, ArH); 7.35 (3H, m, ArH) ppm. ^{19}F NMR δ: −40.3 (s, CF_3) ppm. ^{13}C NMR δ: 13.8 (CH_3); 14.1 (CH_3); 35.1 (*C*HPh); 36.0 (*C*HCO$_2$Et); 61.8 (*OC*H$_2$); 62.7 (*OC*H$_2$); 128.2 (ArC); 128.4 (2C, ArC); 128.8 (2C, ArC); 129.4 (q, $J_{CF} = 311$ Hz, CF_3); 132.2 (quaternary ArC); 167.3 (C=O); 167.6 (C=O) ppm. IR (CCl_4) 1160; 1304; 1042; 1470; 1753; 1732 cm^{-1}. MS (EI) *m*/*z*: 362 ($M^{+\bullet}$, 5); 289 (11); 215 (13); 147 (100%).

Diethyl 2,4-bis(trifluoromethylthio)-3-phenyl-pentan-1,5-dioate (**4**). Stereoisomer **4a**: oil. HRMS 464.0551, $C_{17}H_{18}F_6O_4S_2$ requires 464.0550. ^{1}H NMR δ: 1.02 (3H, t, $J = 7.1$ Hz, CH_3); 1.27 (3H, t, $J = 7.1$ Hz, CH_3); 3.9 (1H, dd, 1H, $J = 10.5$ and 5.6 Hz, H-3); 3.99 (2H, q, $J = 7.1$ Hz, OCH_2); 4.23 (2H, q, $J = 7.1$ Hz, OCH_2); 4.46 (1H, d, $J = 10.5$ Hz, H-2 or H-4); 4.6 (1H, d, $J = 5.6$ Hz, H-4 or H-2); 7.15 (2H, m, ArH); 7.3 (3H, m, ArH) ppm. ^{19}F NMR δ: −40.4 (s, CF_3); −41.0 (s, CF_3) ppm. ^{13}C NMR δ: 13.5 (CH_3); 13.8 (CH_3); 47.5 (C-3); 48.4 (q, $^3J_{CF} = 1.7$ Hz, C-2 or C-4); 49.3 (q, $^3J_{CF} = 1.7$ Hz, C-4 or C-2); 62.2 (OCH_2); 62.6 (m, OCH_2); 128.6 (2C, ArC); 128.7 (2C, ArC); 129.0 (ArC); 129.5 (q, $^1J_{CF} = 308$ Hz, CF_3); 129.7 (q, $^1J_{CF} = 308$ Hz, CF_3); 133.9 (quaternary ArC); 168.7 (C=O); 168.9 (C=O) ppm. IR (CCl_4) 1037; 1138; 1165; 1748 cm^{-1}. MS (EI) *m*/*z*: 464 ($M^{+\bullet}$, 5); 317 (17); 277 (49); 205 (55); 135 (97); 115 (100%). MS (CI, NH_3) *m*/*z*: 482 ($M + NH_4^+$, 90); 465 ($M + H^+$, 100%). Stereoisomer **4b**: oil. ^{1}H NMR δ: 1.1 (6H, t, $J = 7.1$ Hz, CH_3); 3.6 (1H, t, $J = 7.9$ Hz, H-3); 4.05 (4H, q, $J = 7.1$ Hz, OCH_2); 4.74 (2H, d, $J = 7.9$ Hz, H-2 and H-4); 7.29 (5H, m, ArH) ppm. ^{19}F NMR δ: −40.42 (s, CF_3) ppm. ^{13}C NMR δ: 13.6 (CH_3); 48.6 (q, $^3J_{CF} = 1.7$ Hz, C-2 and C-4); 50.0 (C-3); 62.3 (OCH_2); 128.5 (2C, ArC); 128.9 (1C, ArC); 129.1 (2C, ArC); 129.8 (q, $^1J_{CF} = 308$ Hz, CF_3); 133.9 (quaternary ArC); 168.3 (C=O) ppm. MS (EI) *m*/*z*: 464 ($M^{+\bullet}$, 3.5); 317 (26); 277 (100%).

Stereoisomer **4c**: oil. ^{1}H NMR δ: 1.28 (6H, t, $J = 7.1$ Hz, CH_3); 4.07 (2H, t, $J = 8$ Hz, H-3); 4.23 (4H, m, OCH_2); 4.36 (2H, d, $J = 8$ Hz, H-2 and H-4); 7.1–7.4 (5H, m, ArH). ^{19}F NMR δ: −41.0 (s, CF_3) ppm.

3.2. Preparation of ethyl 2-trifluoromethylthioacrylate derivatives **3a–f**

Piperidine (0.13 ml, 1.3 mmol) was added to a solution of ethyl (trifluoromethylthio)acetate (**2**) (0.5 g, 2.7 mmol) and an aldehyde **1** (2.7 mmol) in acetonitrile (20 ml). The mixture was refluxed for 48 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel; pentane/dichloromethane solvent gradient).

Ethyl 3-phenyl-2-(trifluoromethylthio)acrylate (**3a**). *Z*-isomer: oil; bp (Siwoloboff) 242°C. Found C 52.16, H 3.99, $C_{12}H_{11}F_3O_2S$ requires C 52.17, H 4.01. ^{1}H NMR δ: 1.4 (3H, t, $J = 7.0$ Hz, CH_3); 4.3 (2H, q, $J = 7$ Hz, CH_2); 7.45 (3H, m, ArH); 7.85 (2H, m, ArH); 8.4 (1H, s, =CH) ppm. ^{19}F NMR δ: −41.3 (s, CF_3) ppm. ^{13}C NMR (proton-coupled) δ: 14.0 (qt, $^1J_{CH} = 127.5$, $^2J_{CH} = 2.5$ Hz, *C*H_3); 62.4 (tq, $^1J_{CH} = 148.4$, $^2J_{CH} = 4.4$ Hz, *C*H_2); 116.3 (d, $^4J_{CF} = 2.1$ Hz, =*C*–SCF_3); 128.5 (dm, $^1J_{CH} = 170$ Hz, *m*-ArC); 129.1 (qd, $^1J_{CF} = 311$, $^4J_{CH} = 1.7$ Hz, *C*F_3); 131.1 (dt, $^1J_{CH} = 161$, $^2J_{CH} = 7.5$ Hz, *o*-ArC); 131.3 (dm, $^1J_{CH} =$ 161 Hz, *p*-ArC); 133.1 (td, $^2J_{CH} = 6$ and 2 Hz, quaternary ArC); 153.4 (dt, $^1J_{CH} = 155.3$, $^3J_{CH} = 4.4$ Hz, =CH); 165.4 (dt, $^3J_{CH} = 6$ and 2.8 Hz, *C*=O) ppm. IR (CCl_4) 1042; 1143; 1609; 1727 cm^{-1}. MS (EI) *m/z*: 276 ($M^{+\bullet}$, 19); 134 (100%). HRMS found 276.0439, $C_{12}H_{11}F_3O_2S$ requires 276.0432.

E-isomer: spectral parameters for the *E* isomer were obtained on an enriched chromatographic fraction still containing the *Z*-isomer. ^{1}H NMR δ: 1.2 (3H, t, $J =$ 7.0 Hz, CH_3); 4.3 (2H, q, $J = 7.0$ Hz, CH_2); 7.45 (3H, m, ArH); 7.5 (1H, s, vinyl); 7.85 (2H, m, ArH) ppm. ^{19}F NMR δ: −42.7 (s, CF_3) ppm; ^{13}C NMR (proton-coupled) δ: 13.6 (qt, $^1J_{CH} = 127.4$, $^2J_{CH} = 2.6$ Hz, *C*H_3); 62.1 (tq, $^1J_{CH} =$ 148, $^2J_{CH} = 5$ Hz, O*C*H_2); 117.8 (m, =*C*–SCF_3); 128.8 (dm, $^1J_{CH} = 156$ Hz, ArC); 129.2 (qd, $^1J_{CF} = 306$, $^4J_{CH} = 2$ Hz, *C*F_3); 130.2 (dm, $^1J_{CH} = 166$ Hz, ArC); 133.3 (m, ArC); 133.8 (m, quaternary ArC); 150.0 (d, $^1J_{CH} = 160$ Hz, =*C*H); 166.0 (d, $^3J_{CH} = 12$ Hz, *C*=O) ppm.

Ethyl 3-furyl-2-(trifluoromethylthio)acrylate (*Z*) (**3b**). White solid; mp 31.9–32.3°C. Found C 45.11, H 3.43, $C_{10}H_9F_3O_3S$ requires C 45.11, H 3.41%. ^{1}H NMR δ: 1.4 (3H, t, $J = 7.0$ Hz, CH_3); 4.3 (2H, q, $J = 7$ Hz, CH_2); 6.6 (1H, dd, $J = 4$ and 2 Hz, 4-furyl-H); 7.5 (1H, d, $J = 4$ Hz, 3-furyl-H); 7.7 (1H, d, $J = 2$ Hz, 5-furyl-H); 8.2 (1H, s, =CH). ^{19}F NMR δ: −41.4 (s, CF_3) ppm. ^{13}C NMR (proton coupled) δ: 14.0 (qt, $^1J_{CH} = 127$, $^2J_{CH} = 2.5$ Hz, *C*H_3); 62.2 (tq, $^1J_{CH} = 148$, $^2J_{CH} = 4$ Hz, *C*H_2); 113.3 (ddd, $^1J_{CH} = 178$, $^2J_{CH} = 13$, $^3J_{CH} = 4$ Hz, 4-furyl-C); 120.0 (dq, $^1J_{CH} = 179$, $J_{CH} = 6$ Hz, 3-furyl-C); 128.9 (qd, $^1J_{CF} = 311$, $^4J_{CH} =$ 1.5 Hz, *C*F_3); 140.0 (d, $^1J_{CH} = 157$ Hz, =*C*H); 146.7 (ddd, $^1J_{CH} = 204$, $^2J_{CH} = 10$, $^3J_{CH} = 2.5$ Hz, 5-furyl-C); 149.7 (dtd, $^2J_{CH} = 8$, $^3J_{CH} = 7.6$, $^4J_{CH} = 1.7$ Hz, 2-furyl-C); 152.2 (s, =*C*–SCF_3); 165.0 (dt, $^3J_{CH} = 5$, $^2J_{CH} = 6$ Hz, *C*=O). IR (CCl_4) 1732; 1721; 1620; 1149; 1170; 1054 cm^{-1}. MS (EI) *m/z*: 266 ($M^{+\bullet}$, 97); 221 (20); 124 (100%).

Ethyl *trans*-3-cinnamyl-2-(trifluoromethylthio)acrylate (*Z*) (**3c**). Oil, bp (Siwoloboff) 295°C (dec.). Found C 55.65, H 4.37, $C_{14}H_{13}F_3O_2S$ requires C 55.62, H 4.33%. ^{1}H NMR δ: 1.4 (3H, t, $^3J_{HH} = 7.1$ Hz, CH_3); 4.4 (2H, q, $^3J_{HH} = 7.1$ Hz, CH_2O); 7.18 (1H, d, $^3J_{HH} = 16$ Hz, =CHPh); 7.4 (3H, m, ArH); 7.5 (1H, dd, $^3J_{HH} = 11$ and 16 Hz, *H*C=CHPh); 7.6 (2H, m, ArH); 8.15 (1H, d, $^3J_{HH} = 11$ Hz, =C*H*–CH=CHPh) ppm. ^{19}F NMR δ: −42.2 (s, CF_3) ppm. ^{13}C NMR (proton-coupled) δ: 14.1 (qt, $^1J_{CH} = 127$, $^2J_{CH} = 2.5$ Hz, CH_3); 62.0 (tq, $^1J_{CH} = 144$, $^2J_{CH} = 5$ Hz, CH_2O); 115.0 (s, =C–SCF_3); 124 (d, $^1J_{CH} = 153$ Hz, H*C*=CHPh); 128.0 (dm, $^1J_{CH} = 159$ Hz, *m*-ArC); 128.9 (dd, $^1J_{CH} = 161$, $^2J_{CH} = 7$ Hz, *o*-ArC); 129 (q, $^1J_{CF} = 311$ Hz, CF_3); 130.2 (dt, $^1J_{CH} = 162$, $^2J_{CH} = 8$ Hz, p-ArC); 135.4 (m, quaternary ArC); 146.0 (dm, $^1J_{CH} = 156$ Hz, =*C*HPh); 154.7 (dd, $^1J_{CH} = 156$, $^2J_{CH} = 8$ Hz, =CH–HC=CHPh); 165.0 (dt, $^3J_{CH} = 5$ and 3 Hz, C=O) ppm; IR (CCl_4) 1732; 1710; 1620; 1165; 1143; 1047 cm^{-1}. MS (EI) *m/z*: 302 ($M^{+\bullet}$, 50); 257 (15); 233 (52); 161 (100%).

Ethyl 3-(3-methoxyphenyl)-2-(trifluoromethylthio)acrylate (*Z*) (**3d**). Oil, bp (Siwoloboff) 278–280°C. HRMS Found 306.0535, $C_{13}H_{13}F_3O_3S$ requires 306.0538; ^{1}H NMR (benzene d6) δ: 1.03 (3H, t, $J = 7.1$ Hz, CH_3); 3.27 (3H, s, OCH_3); 4.08 (2H, q, $J = 7.1$ Hz, CH_2O); 6.72 (1H, dd, 1H, $J = 8.3$ and 1.9 Hz, 6′-ArH); 6.97 (1H, t, $J = 8.1$ Hz, 5′-ArH); 7.13 (1H, m, 1H, 4′-ArH); 7.29 (1H, s, 3′-ArH); 8.36 (1H, s, =CH) ppm. ^{19}F NMR (benzene d6) δ: −41.5 (s, CF_3) ppm. ^{13}C NMR (proton-coupled, benzene d6) δ: 14.0 (qt, $^1J_{CH} = 127.1$, $^2J_{CH} = 2.6$ Hz, CH_3); 54.7 (q, $^1J_{CH} = 144$ Hz, OCH_3); 62.3 (tq, $^1J_{CH} = 148$, $^2J_{CH} =$ 4.4 Hz, CH_2); 116.0 (dq, $^1J_{CH} = 160$, $^2J_{CH} = 5.5$ Hz, 2′-ArC); 116.8 (m, $^3J_{CF} = 2$ Hz, =*C*–SCF_3); 117.7 (ddd, $^1J_{CH} = 162$, $^2J_{CH} = 4.9$, $^3J_{CH} = 4.6$ Hz, 4′-ArC); 124.3 (dq, $^1J_{CH} = 163$, $^3J_{CH} = 6$ Hz, 6′-ArC); 130.0 (qd, $^1J_{CF} =$ 315.5, $^4J_{CH} = 2$ Hz, CF_3); 129.7 (dd, $^1J_{CH} = 160$, $^2J_{CH} = 2$ Hz, 5′-ArC); 134.7 (d, $^2J_{CH} = 9$ Hz, 1′-ArC); 153.7 (dt, $^1J_{CH} = 155$, $^3J_{CH} = 4.6$ Hz, =CH); 159.9 (m, 3′-ArC); 165.0 (dt, $^3J_{CH} = 3$ and 6 Hz, C=O) ppm. IR (CCl_4) 1732; 1710; 1614; 1160; 1047 cm^{-1}. MS (EI) *m/z*: 306 ($M^{+\bullet}$, 57); 261 (14); 237 (45); 164 (100%).

Ethyl 3-(2-naphthyl)-2-(trifluoromethylthio)acrylate (*Z*) (**3e**). White solid, mp = 41.7–51.1°C. Found C 59.08, H 4.07, $C_{16}H_{13}F_3O_2S$ requires C 58.89, H 4.02%. ^{1}H NMR δ: 1.4 (3H, t, $J = 7.1$ Hz, CH_3); 4.4 (2H, q, $J = 7.1$ Hz, CH_2O); 7.55 (2H, m, 2H, 6′- and 7′-ArH); 7.8 (3H, m, ArH); 8.1 (1H, m, 3′-ArH); 8.25 (1H, s, 1′-ArH); 8.6 (1H, s, =CH–) ppm. ^{19}F NMR δ: −41.4 (s, CF_3) ppm. ^{13}C NMR (proton-coupled) δ: 14.0 (qt, $^1J_{CH} = 127$, $^2J_{CH} = 2.5$ Hz, CH_3); 62.4 (tq, $^1J_{CH} = 148$, $^2J_{CH} = 4$ Hz, OCH_2); 115.9 (d, $^2J_{CH} = 2$ Hz, =*C*–SCF_3); 126.7 (dd, $^1J_{CH} = 160$, $^3J_{CH} =$ 8 Hz, 6′- and 7′-ArC); 127.6 (dm, $^1J_{CH} = 162$ Hz, ArC); 128.0 (dm, $^1J_{CH} = 161$ Hz, ArC); 128.1 (dm, $^1J_{CH} =$ 159 Hz, ArC); 128.9 (dm, $^1J_{CH} = 162$ Hz, 3′-ArC); 129.1 (q, $^1J_{CF} = 311$ Hz, CF_3); 130.6 (d, $^1J_{CH} = 9$ Hz, 2′-ArC); 132.7 (m, 10′-ArC); 133.4 (dq, $^1J_{CH} = 159$, $^3J_{CH} = 5.5$ Hz,

1′-ArC); 134.3 (m, 9′-ArC); 153.4 (dt, $^{1}J_{CH} = 155$, $^{3}J_{CH} = 4.5$ Hz, =CH–); 165.5 (dt, $^{3}J_{CH} = 6$ and 3 Hz, C=O) ppm. IR (CCl_4) 1732; 1711; 1170; 1604; 1138; 1042 cm^{-1}. MS (EI) *m/z*: 326 ($M^{+\bullet}$, 39); 185 (100%).

Ethyl 3-propyl-2-(trifluoromethylthio)acrylate (*Z*) (**3f**). Oil, bp 71°C/10 mm Hg. Found C 44.72, H 5.37, S 13.34, $C_{12}H_{11}F_3O_2S$ requires C 44.62, H 5.41, S 13.24%. ^{1}H NMR δ: 0.98 (3H, t, $J = 7.4$ Hz, $CH_3CH_2CH_2$); 1.33 (3H, t, $J = 7.1$ Hz, CH_3CH_2O); 1.55 (2H, sextuplet, $J = 7.4$ Hz, $CH_3CH_2CH_2$); 2.57 (2H, q, $J = 7.5$ Hz, $CH_3CH_2CH_2$); 4.3 (2H, q, $J_{HH} = 7.1$ Hz, CH_3CH_2O); 7.7 (1H, t, $J = 7.5$ Hz, =CH–) ppm. ^{19}F NMR δ: −42.2 (s, CF_3) ppm. ^{13}C NMR (proton-coupled) δ: 13.8 (qt, $^{1}J_{CH} = 125$, $^{2}J_{CH} = 4.2$ Hz, CH_3); 14.0 (qt, $^{1}J_{CH} = 127$, $^{2}J_{CH} = 2.7$ Hz, CH_3); 21.3 (tm, $^{1}J_{CH} = 127$ Hz, $CH_3CH_2CH_2$); 33.3 (tm, $^{1}J_{CH} = 129$ Hz, $CH_3CH_2CH_2$); 62.1 (tq, $^{1}J_{CH} = 148$, $^{2}J_{CH} = 4.5$ Hz, CH_2O); 119.1 (m, $^{3}J_{CF} = 2$ Hz, =C–SCF_3); 129.1 (qd, $^{1}J_{CF} = 310$, $^{3}J_{CH} = 1.7$ Hz, CF_3); 161.4 (dm, $^{1}J_{CH} = 156$ Hz, =CH–); 164.5 (dt, $^{3}J_{CH} = 4.6$ and 2.2 Hz, C=O) ppm. IR (CCl_4) 1727; 1716; 1625; 1475; 1448; 1304; 1283; 1170; 1053 cm^{-1}. MS (EI) *m/z*: 242 ($M^{+\bullet}$, 2.5); 169 (23); 141 (68); 67 (100%).

*3.3. Preparation of ethyl 2-(trifluoromethylthio)acrylate (**3g**)*

An excess of formaldehyde (0.16 mol), produced by pyrolysis of paraformaldehyde, was introduced as vapour via a side arm into a solution of ethyl (trifluoromethylthio)acetate (**2**) (2 g, 10.6 mmol) and piperidine (1.81 g, 21.2 mmol) in acetonitrile (50 ml). The mixture was stirred for 4 days at room temperature. Water was added and the solution was extracted with diethyl ether. The organic layer was washed with brine and dried over magnesium sulfate. After removal of the solvent under reduced pressure, the residue, which showed a peak in the ^{19}F NMR spectrum at δ −37 ppm attributed to the piperidine addition compound **6**, was purified by column chromatography (silica gel; dichloromethane as eluent) to give 0.77 g (36%) of ethyl (trifluoromethylthio)acrylate (**3g**) as an oil. Found C 35.99, H 3.36, S 15.81, $C_6H_7F_3O_2S$ requires C 36.00, H 3.52, S 16.02%. ^{1}H NMR δ: 1.31 (3H, t, $J = 7.1$ Hz, CH_3); 4.27 (2H, q, $J = 7.1$ Hz, CH_2O); 6.36 (1H, s, =CH–); 6.88 (1H, s, =CH–) ppm. ^{19}F NMR δ: −42.5 (s, CF_3) ppm. ^{13}C NMR δ: 13.8 (CH_3); 62.4 (CH_2O); 128.1 (q, $^{3}J_{CF} = 2.1$ Hz, =C–SCF_3); 129.0 (q, $^{1}J_{CF} = 308$ Hz, CF_3); 137.2 (d, $^{4}J_{CF} = 1.1$ Hz, CH_2=); 163.2 (d, $^{4}J_{CF} = 0.9$ Hz, C=O) ppm. IR (CCl_4) 1737; 1731; 1293; 1176; 1149; 1101 cm^{-1}. MS (EI) *m/z*: 200 ($M^{+\bullet}$, 45); 155 (26); 131 (23); 127 (77); 69 (34); 58 (100%).

4. Conclusion

We have shown that ethyl 2-(trifluoromethylthio)acrylate could be prepared under mild conditions by Knoevenagel condensation of ethyl 2-(trifluoromethylthio)acetate with formaldehyde. Using the same conditions with higher aldehydes we obtained ethyl 3-aryl or 3-alkyl-2-(trifluoromethylthio)acrylates with high *Z*-stereoselectivity.

Acknowledgements

This work enters in the frame of the European TMR programme ERB FMRX-CT970120, entitled ‘Fluorine As a Unique Tool for Engineering Molecular Properties’.

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